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                Pharmacokinetic information and systematic chemical names
                 added to PHAR
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                 right truncation
NEWS 21 Jun 06 Simultaneous left and right truncation added to CBNB
NEWS 22 Jun 06 PASCAL enhanced with additional data
NEWS 23 Jun 20 2003 edition of the FSTA Thesaurus is now available
NEWS 24 Jun 25 HSDB has been reloaded
NEWS 25 Jul 16 Data from 1960-1976 added to RDISCLOSURE
NEWS 26 Jul 21 Identification of STN records implemented
NEWS 27 Jul 21 Polymer class term count added to REGISTRY
NEWS 28 Jul 22 INPADOC: Basic index (/BI) enhanced; Simultaneous Left and
                 Right Truncation available
NEWS 29 AUG 05 New pricing for EUROPATFULL and PCTFULL effective
                 August 1, 2003
NEWS 30 AUG 13
                 Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 31 AUG 15
                 PATDPAFULL: one FREE connect hour, per account, in
                 September 2003
NEWS 32
        AUG 15
                 PCTGEN: one FREE connect hour, per account, in
                 September 2003
NEWS 33 AUG 15
                RDISCLOSURE: one FREE connect hour, per account, in
                 September 2003
NEWS 34 AUG 15
                 TEMA: one FREE connect hour, per account, in
                 September 2003
NEWS 35 AUG 18 Data available for download as a PDF in RDISCLOSURE
NEWS 36 AUG 18 Simultaneous left and right truncation added to PASCAL
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NEWS 37 AUG 18 FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation

NEWS 38 AUG 18 Simultaneous left and right truncation added to ANABSTR

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MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003

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=> s heat(w)shock(w)protein# or hsp###

14866 HEAT(W) SHOCK(W) PROTEIN# OR HSP###

=> s soluble(5a)12

126 SOLUBLE (5A) L2 T.3

=> s 11 and 13

20 L1 AND L3

=> d ibib tot

ANSWER 1 OF 20 PCTFULL ACCESSION NUMBER:

TITLE (ENGLISH):

TITLE (FRENCH): INVENTOR(S):

COPYRIGHT 2003 Univentio on STN 2003068822 PCTFULL ED 20030903 EW 200334 DE-IMMUNIZED (POLY) PEPTIDE CONSTRUCTS

CONSTRUCTIONS (POLY) PEPTIDIQUES DESIMMUNISEES ZOCHER, Marcel, Friedrich-Heckerstr. 34, D-79539

Loerrach, DE [DE, DE];

DREIER, Torsten, Johann-Clanze-Strasse 39, D-81369

Muenchen, DE [DE, DE];

BAeUERLE, Patrick, Waldpromenade 18C, D-82131 Gauting,

DE [DE, DE]

MICROMET AG, Staffelseestrasse 2, D-81477 Muenchen, DE PATENT ASSIGNEE(S):

[DE, DE], for all designates States except US; ZOCHER, Marcel, Friedrich-Heckerstr. 34, D-79539

Loerrach, DE [DE, DE], for US only; DREIER, Torsten, Johann-Clanze-Strasse 39, D-81369

Muenchen, DE [DE, DE], for US only;

BAeUERLE, Patrick, Waldpromenade 18C, D-82131 Gauting, DE [DE, DE], for US only

AGENT:

VOSSIUS & PARTNER\$, Siebertsrasse 4, D-81765 Muenchen\$,

LANGUAGE OF FILING: LANGUAGE OF PUBL.:

DOCUMENT TYPE:

English English Patent

PATENT INFORMATION:

NUMBER KIND DATE WO 2003068822 A2 20030821

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD

MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW RW (ARIPO):

AM AZ BY KG KZ MD RU TJ TM RW (EAPO):

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU RW (EPO):

MC NL PT SE SI SK TR

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG RW (OAPI):

APPLICATION INFO .: PRIORITY INFO.:

WO 2003-EP1389 A 20030212 EP 2002-02003332.0 20020213

ANSWER 2 OF 20 ACCESSION NUMBER:

TITLE (ENGLISH):

TITLE (FRENCH):

INVENTOR(S):

PCTFULL COPYRIGHT 2003 Univentio on STN 2003042661 PCTFULL ED 20030530 EW 200321 METHODS OF DIAGNOSIS OF CANCER, COMPOSITIONS AND METHODS OF SCREENING FOR MODULATORS OF CANCER

METHODES DE DIAGNOSTIC DU CANCER, COMPOSITIONS ET METHODES DE CRIBLAGE DES MODULATEURS DU CANCER

AFAR, Daniel, 435 Visitacion Avenue, Brisbane, CA 94005, US [CA, US];

AZIZ, Natasha, 411 California Avenue, Palo Alto, CA 94306, US [US, US];

GINSBURG, Wendy, M., 655 Page Street, San Francisco, CA 94117, US [US, US];

GISH, Kurt, C., 37 Artuna Avenue, Piedmont, CA 94611, US [US, US];

GLYNNE, Richard, 2691 Palomino Circle, La Jolla, CA 92037, US [GB, US];

HEVEZI, Peter, A., 1360 11th Avenue, San Francisco, CA 94122, US [GB, US];

MACK, David, H., 2076 Monterey Avenue, Menlo Park, CA 94025, US [US, US];

MURRAY, Richard, 22643 Woodridge Court, Cupertino, CA 95014, US [US, US];

WATSON, Susan, R., 805 Balra Drive, El Cerrito, CA 94530, US [GB, US];

WILSON, Keith, E., 219 Jeter Street, Redwood City, CA 94062, US [US, US];

ZLOTNIK, Albert, 507 Alger Drive, Palo Alto, CA 94306, US [US, US]

PATENT ASSIGNEE(S):

EOS BIOTECHNOLOGY, INC., 225A Gateway Boulevard, South San Francisco, CA 94080, US [US, US], for all designates States except US; AFAR, Daniel, 435 Visitacion Avenue, Brisbane, CA

94005, US [CA, US], for US only; AZIZ, Natasha, 411 California Avenue, Palo Alto, CA 94306, US [US, US], for US only;

GINSBURG, Wendy, M., 655 Page Street, San Francisco, CA 94117, US [US, US], for US only;

GISH, Kurt, C., 37 Artuna Avenue, Piedmont, CA 94611, US [US, US], for US only;

GLYNNE, Richard, 2691 Palomino Circle, La Jolla, CA 92037, US [GB, US], for US only;

HEVEZI, Peter, A., 1360 11th Avenue, San Francisco, CA 94122, US [GB, US], for US only;

MACK, David, H., 2076 Monterey Avenue, Menlo Park, CA 94025, US {US, US], for US only; MURRAY, Richard, 22643 Woodridge Court, Cupertino, CA

95014, US [US, US], for US only;

WATSON, Susan, R., 805 Balra Drive, El Cerrito, CA 94530, US [GB, US], for US only;

WILSON, Keith, E., 219 Jeter Street, Redwood City, CA 94062, US [US, US], for US only;

ZLOTNIK, Albert, 507 Alger Drive, Palo Alto, CA 94306, US [US, US], for US only

BASTIAN, Kevin, L.\$, Townsend and Townsend and Crew LLP, Two Embarcadero Center, Eighth Floor, San

Francisco, CA 94111\$, US

English English

Patent

AGENT:

LANGUAGE OF FILING: LANGUAGE OF PUBL.: DOCUMENT TYPE: PATENT INFORMATION:

WO 2003042661 A2 20030522 DESIGNATED STATES AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR W: CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW RW (ARIPO): AM AZ BY KG KZ MD RU TJ TM RW (EAPO): RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR RW (OAPI): BF BJ CF CG CI CM GA GN GO GW ML MR NE SN TD TG WO 2002-US36810 A 20021113 APPLICATION INFO.: PRIORITY INFO.: US 2001-60/350,666 20011113 US 2001-60/332,464 20011121 US 2001-60/334,393 20011129 US 2001-60/335,394 20011203 US 2001-60/340,376 20011214 US 2002-60/347,211 20020108 US 2002-60/347,349 20020110 20020208 US 2002-60/347,349 US 2002-60/356,714 20020213 US 2002-60/359,077 20020220 US 2002-60/368,809 20020329 US 2002-60/370,110 20020404 US 2002-60/372,246 20020412 US 2002-60/386,614 20020605 US 2002-60/396,839 20020716 US 2002-60/397,775 20020722 US 2002-60/397,845 20020722 US 2002-60/409,450 20020909 ANSWER 3 OF 20 COPYRIGHT 2003 Univentio on STN PCTFULL 2003025138 PCTFULL ED 20030402 EW 200313 ACCESSION NUMBER: METHODS OF DIAGNOSIS OF CANCER COMPOSITIONS AND METHODS TITLE (ENGLISH): OF SCREENING FOR MODULATORS OF CANCER PROCEDES DE DIAGNOSTIC DU CANCER, COMPOSITIONS ET TITLE (FRENCH): PROCEDES DE CRIBLAGE DE MODULATEURS DU CANCER INVENTOR(S): AFAR, Daniel, 435 Visitacion Avenue, Brisbane, CA 94005, US [CA, US]; AZIZ, Natasha, 411 California Avenue, Palo Alto, CA 94306, US [US, US]; GISH, Kurt, C., 37 Artuna Avenue, Piedmont, CA 94611, US [US, US]; HEVEZI, Peter, A., 1360 11th Avenue, San Francisco, CA 94122, US [GB, US]; MACK, David, H., 2076 Monterey Avenue, Menlo Park, CA 94025, US [US, US]; WILSON, Keith, E., 219 Jeter Street, Redwood City, CA 94062, US [US, US]; ZLOTNIK, Albert, 507 Alger Drive, Palo Alto, CA 94306, US [US, US] PATENT ASSIGNEE(S): EOS BIOTECHNOLOGY, INC., 225A Gateway, Boulevard, South San Francisco, CA 94080, US [US, US], for all designates States except US; AFAR, Daniel, 435 Visitacion Avenue, Brisbane, CA

94005, US [CA, US], for US only;

94306, US [US, US], for US only;

AZIZ, Natasha, 411 California Avenue, Palo Alto, CA

GISH, Kurt, C., 37 Artuna Avenue, Piedmont, CA 94611,

KIND

NUMBER

DATE

US [US, US], for US only;
HEVEZI, Peter, A., 1360 11th Avenue, San Francisco, CA
94122, US [GB, US], for US only;
MACK, David, H., 2076 Monterey Avenue, Menlo Park, CA
94025, US [US, US], for US only;
WILSON, Keith, E., 219 Jeter Street, Redwood City, CA
94062, US [US, US], for US only;
ZLOTNIK, Albert, 507 Alger Drive, Palo Alto, CA 94306,
US [US, US], for US only
BASTIAN, Kevin, L.\$, Townsend and Townsend and Crew
LLP, Two Embarcadero Center, Eighth Floor, San
Francisco, CA 94111\$, US
English

LANGUAGE OF FILING: LANGUAGE OF PUBL.: DOCUMENT TYPE: PATENT INFORMATION:

AGENT:

NUMBER KIND DATE
----WO 2003025138 A2 20030327

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZW ZW

RW (ARIPO): GH GM KE LS·MW MZ SD SL SZ TZ UG ZM ZW RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

English

Patent

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC

NL PT SE SK TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.:
PRIORITY INFO.:

RW (EPO):

WO 2002-US29560 A 20020917 US 2001-60/323,469 20010917 US 2001-60/323,887 20010920 US 2001-60/355,1666 20011113 US 2002-60/355,145 20020208 US 2002-60/355,257 20020208 US 2002-60/372,246 20020412

L4 ANSWER 4 OF 20 ACCESSION NUMBER: TITLE (ENGLISH): TITLE (FRENCH): PCTFULL COPYRIGHT 2003 Univentio on STN 2002034205 PCTFULL ED 20020515 EW 200218 USING HEAT SHOCK PROTEINS TO INCREASE IMMUNE RESPONSE

UTILISATION DES PROTEINES DU STRESS POUR STIMULER LA REPONSE IMMUNITAIRE

INVENTOR(S): SRIVASTAVA, Pramod, K., 70 Pheasent Run, Avon, CT

PATENT ASSIGNEE(S):

UNIVERSITY OF CONNECTICUT HEALTH CENTER, 263 Farmington Avenue, Farmington, CT 06030, US [US, US]

ANTLER, Adriane, M.\$, Pennie & Edmonds LLP, 1155 Avenue

AGENT:

of the Americas, New York, NY 10036\$, US English

LANGUAGE OF FILING: LANGUAGE OF PUBL.: DOCUMENT TYPE: PATENT INFORMATION:

English Patent

DESIGNATED STATES

W: RW (EPO): AU CA JP

AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

TR
APPLICATION INFO:: WO 2001-US46332 A 20011019
PRIORITY INFO:: US 2000-09/693,643 20001020

PCTFULL COPYRIGHT 2003 Univentio on STN ANSWER 5 OF 20 ACCESSION NUMBER: 2002016414 PCTFULL ED 20020711 EW 200209 TITLE (ENGLISH): COMPOSITION FOR THE ELIMINATION OF AUTOREACTIVE B-CELLS COMPOSITION DESTINEE A L'ELIMINATION DES CELLULES B TITLE (FRENCH): AUTOREACTIVES ZOCHER, Marcel, Theodor-Koerner-Str. 13, 82049 INVENTOR(S): Muenchen-Pullach, DE [DE, DE]; BAeUERLE, Patrick, Vogelsangstr. 13A, 82152 Gauting, DE [DE, DE]; DREIER, Torsten, Johann-Clanze-Str. 39, 81369 Muenchen, DE [DE, DE] MICROMET AG, Am Klopferspitz 19, 82152 PATENT ASSIGNEE(S): Martinsried/Muenchen, DE [DE, DE], for all designates States except US; ZOCHER, Marcel, Theodor-Koerner-Str. 13, 82049 Muenchen-Pullach, DE [DE, DE], for US only; BAeUERLE, Patrick, Vogelsangstr. 13A, 82152 Gauting, DE [DE, DE], for US only; DREIER, Torsten, Johann-Clanze-Str. 39, 81369 Muenchen, DE [DE, DE], for US only AGENT: VOSSIUS & PARTNER\$, Sieberstr. 4, 81675 Muenchen\$, DE LANGUAGE OF FILING: English English LANGUAGE OF PUBL.: DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE ______ WO 2002016414 A2 20020228 DESIGNATED STATES AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR W: CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW RW (ARIPO): GH GM KE L5 mw rd 52 1. RW (EAPO): AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GH GM KE LS MW MZ SD SL SZ TZ UG ZW AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG APPLICATION INFO:: WO 2001-EP9714 A 20010822 PRIORITY INFO:: EP 2000-00117354.1 20000822 ANSWER 6 OF 20 PCTFULL COPYRIGHT 2003 Univentio on STN ACCESSION NUMBER: 2001064835 PCTFULL ED 20020822 TITLE (ENGLISH): NOVEL NUCLEIC ACIDS AND POLYPEPTIDES TITLE (FRENCH): NOUVEAUX ACIDES NUCLEIOUES ET POLYPEPTIDES INVENTOR(S): TANG, Y., Tom; LIU, Chenghua; DRMANAC, Radoje, T. HYSEQ, INC.; PATENT ASSIGNEE(S): TANG, Y., Tom; LIU, Chenghua; DRMANAC, Radoje, T. DOCUMENT TYPE: Patent

PATENT INFORMATION:

į

NUMBER KIND DATE
----WO 2001064835 A2 20010907

DESIGNATED STATES W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM

TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF

CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO .: PRIORITY INFO.:

WO 2001-US4927 A 20010226 US 2000-09/515,126 20000228 US 2000-09/577,409 20000518

ANSWER 7 OF 20 L4

PCTFULL COPYRIGHT 2003 Univentio on STN 1999047169 PCTFULL ED 20020515

ACCESSION NUMBER: TITLE (ENGLISH): TITLE (FRENCH):

METHODS TO PROVOKE ANTI-CANCER IMMUNE RESPONSES METHODES POUR PROVOQUER DES REPONSES IMMUNITAIRES

ANTICANCEREUSES

INVENTOR(S):

INVENTOR(S): ROBERTS, Bruce, L. PATENT ASSIGNEE(S): GENZYME CORPORATION; ROBERTS, Bruce, L.

LANGUAGE OF PUBL.: DOCUMENT TYPE:

English Patent

PATENT INFORMATION:

NUMBER KIND DATE _____ WO 9947169 Al 19990923

DESIGNATED STATES W:

AU CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU

MC NL PT SE

APPLICATION INFO.: PRIORITY INFO.:

A 19990319 WO 1999-US6048 US 1998-60/078,931 19980320

ANSWER 8 OF 20

PCTFULL COPYRIGHT 2003 Univentio on STN

ACCESSION NUMBER: 1999027958 PCTFULL ED ZUUZUDID
TITLE (ENGLISH): HIV-1 TAT, OR DERIVATIVES THEREOF FOR PROPHYLACTIC AND

TITLE (FRENCH):

TAT DE VIH-1 OU SES DERIVES COMME PRODUIT PROPHYLACTIQUE OU THERAPEUTIQUE DE VACCINATION

INVENTOR(S): ENSOLI, Barbara
PATENT ASSIGNEE(S): ISTITUTO SUPERIORE DI SANITA';
ENSOLI, Barbara

LANGUAGE OF PUBL.: DOCUMENT TYPE:

English Patent

PATENT INFORMATION:

NUMBER KIND DATE

WO 9927958 A2 19990610

DESIGNATED STATES

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 1998-EP7721 A 19981130

PRIORITY INFO.:

IT 1997-RM97A000743 19971201

ANSWER 9 OF 20 USPATFULL on STN

ACCESSION NUMBER:

2003:72182 USPATFULL

INVENTOR(S):

Induction of a Th1-like response in vitro Siegel, Marvin, Blue Bell, PA, UNITED STATES

Chu, N. Randall, Victoria, CANADA

PATENT ASSIGNEE(S):

Mizzen, Lee A., Victoria, CANADA Stressgen Biotechnologies Corporation, a Victoria,

Canada corporation (U.S. corporation)

NUMBER KIND DATE _____ ___

PATENT INFORMATION: US 2003050469 A1 20030313
APPLICATION INFO.: US 2002-267311 A1 20021009 (10)

RELATED APPLN. INFO.:

Continuation of Ser. No. US 2000-613303, filed on 10

Jul 2000, GRANTED, Pat. No. US 6495347

NUMBER DATE _____

PRIORITY INFORMATION:

US 1999-143757P 19990708 (60)

DOCUMENT TYPE:

Utility

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE: FISH & RICHARDSON PC, 225 FRANKLIN ST, BOSTON, MA,

02110 64

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 37 Drawing Page(s)

LINE COUNT: 4386

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 10 OF 20 USPATFULL on STN

ACCESSION NUMBER:

2003:40533 USPATFULL

TITLE:

Methods for the inhibition of epstein-barr virus

transmission employing anti-viral peptides capable of

abrogating viral fusion and transmission

INVENTOR(S):

Barney, Shawn O'Lin, Cary, NC, United States Lambert, Dennis Michael, Cary, NC, United States Petteway, Stephen Robert, Cary, NC, United States

PATENT ASSIGNEE(S):

Trimeris, Inc., Durham, NC, United States (U.S.

corporation)

NUMBER KIND DATE _____

PATENT INFORMATION:

US 6518013 B1 20030211

APPLICATION INFO.:

US 1995-485546 19950607 (8)

Continuation-in-part of Ser. No. US 1994-360107, filed RELATED APPLN. INFO.: on 20 Dec 1994, now patented, Pat. No. US 6017536 Continuation-in-part of Ser. No. US 1994-255208, filed

on 7 Jun 1994 Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No.

US 5464933 Utility

DOCUMENT TYPE:

GRANTED

24700

FILE SEGMENT: PRIMARY EXAMINER:

PRIMARY EXAMINER: Scheiner, Laurie ASSISTANT EXAMINER: Parkin, Jeffrey S.

LEGAL REPRESENTATIVE: Pennie & Edmonds LLP, Nelson, M. Bud

NUMBER OF CLAIMS: 22

EXEMPLARY CLAIM:

1

NUMBER OF DRAWINGS:

84 Drawing Figure(s); 83 Drawing Page(s)

LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 11 OF 20 USPATFULL on STN

ACCESSION NUMBER:

2003:30345 USPATFULL

TITLE:

Ligation of CEACAM1

INVENTOR(S):

Gray-Owen, Scott D., Oakville, CANADA

Boulton, Ian C., Toronto, CANADA

NUMBER KIND DATE ______ PATENT INFORMATION: US 2003022292 A1 20030130 APPLICATION INFO.: US 2002-163638 A1 20020607 (10)

NUMBER DATE

PRIORITY INFORMATION: US 2001-296152P 20010607 (60)

DOCUMENT TYPE: Utility

APPLICATION . FILE SEGMENT:

LEGAL REPRESENTATIVE: BERESKIN AND PARR, SCOTIA PLAZA, 40 KING STREET

WEST-SUITE 4000 BOX 401, TORONTO, ON, M5H 3Y2

22 NUMBER OF CLAIMS:

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 23 Drawing Page(s)

LINE COUNT: 2327

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 12 OF 20 USPATFULL on STN

ACCESSION NUMBER:

2002:332610 USPATFULL

TITLE: INVENTOR(S): Induction of a Th1-like response in vitro Siegel, Marvin, Blue Bell, PA, United States

Chu, N. Randall, Victoria, CANADA

Mizzen, Lee A., Victoria, CANADA

PATENT ASSIGNEE(S):

Stressgen Biotechnologies Corporation, Victoria, CANADA

(non-U.S. corporation)

KIND DATE NUMBER ______

PATENT INFORMATION: APPLICATION INFO.:

US 6495347 B1 20021217 US 2000-613303 20000710 20000710 (9)

NUMBER DATE ----

PRIORITY INFORMATION: US 1999-143757P 19990708 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Park, Hankyel T.

LEGAL REPRESENTATIVE: Fish & Richardson P.C.

NUMBER OF CLAIMS: 64

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 39 Drawing Figure(s); 37 Drawing Page(s)

4697 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 13 OF 20 USPATFULL on STN

ACCESSION NUMBER:

2002:307563 USPATFULL

TITLE:

Using heat shock proteins to increase immune response

Srivastava, Pramod K., Avon, CT, UNITED STATES INVENTOR(S): University of Connecticut Health Center (U.S. PATENT ASSIGNEE(S):

corporation)

NUMBER KIND DATE

PATENT INFORMATION: APPLICATION INFO.:

US 2002172682 A1 20021121 US 2002-131937 A1 20020425 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-693643, filed

on 20 Oct 2000, PENDING

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW

YORK, NY, 100362711

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 12 Drawing Page(s)

LINE COUNT: 3533

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 14 OF 20 USPATFULL on STN

ACCESSION NUMBER: 2002:297296 USPATFULL

Methods for inhibition of membrane fusion-associated TITLE:

events, including respiratory syncytial virus

transmission

Bolognesi, Dani Paul, Durham, NC, United States INVENTOR(S):

Matthews, Thomas James, Durham, NC, United States

Wild, Carl T., Durham, NC, United States Barney, Shawn O'Lin, Cary, NC, United States Lambert, Dennis Michael, Cary, NC, United States

Petteway, Stephen Robert, Cary, NC, United States Langlois, Alphonse J., Durham, NC, United States

Trimeris, Inc., Durham, NC, United States (U.S. PATENT ASSIGNEE(S):

corporation)

KIND DATE NUMBER _____ US 6479055 B1 20021112 PATENT INFORMATION:

US 1995-470896 19950606 (8) APPLICATION INFO.: RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994, now patented, Pat. No. US 6017536 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No.

> US 5464933 Utility

DOCUMENT TYPE: FILE SEGMENT: GRANTED PRIMARY EXAMINER:

Stucker, Jeffrey LEGAL REPRESENTATIVE: Pennie & Edmonds LLP

NUMBER OF CLAIMS: 44

EXEMPLARY CLAIM:

84 Drawing Figure(s); 83 Drawing Page(s) NUMBER OF DRAWINGS:

LINE COUNT: 26553

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 15 OF 20 USPATFULL on STN

ACCESSION NUMBER: 2002:112558 USPATFULL

Fungal antigens and process for producing the same TITLE:

INVENTOR(S): Takesako, Kazutoh, Otsu-shi, JAPAN Mizutani, Shigetoshi, Gamo-gun, JAPAN Endo, Masahiro, Kusatsu-shi, JAPAN

Kato, Ikunoshin, Uji-shi, JAPAN

PATENT ASSIGNEE(S): TAKARA SHUZO CO., LTD, Kyoto, JAPAN (non-U.S.

corporation)

NUMBER KIND DATE US 2002058293 A1 20020516 US 2001-987190 A1 20011113 (9) PATENT INFORMATION: APPLICATION INFO.:

RELATED APPLN. INFO.: Division of Ser. No. US 1999-262856, filed on 4 Mar

1999, PENDING

NUMBER DATE _____ WO 1997-JP3041 19970829 JP 1996-255400 19960904 JP 1997-99775 19970331 PRIORITY INFORMATION:

DOCUMENT TYPE: Utility APPLICATION FILE SEGMENT:

LEGAL REPRESENTATIVE: BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS

CHURCH, VA, 22040-0747

NUMBER OF CLAIMS: 20 EXEMPLARY CLAIM: 1

9 Drawing Page(s) NUMBER OF DRAWINGS:

LINE COUNT: 3093

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 16 OF 20 USPATFULL on STN

ACCESSION NUMBER: 2002:12021 USPATFULL In VIVO loading of MHC TITLE:

INVENTOR(S): Roberts, Bruce L., Southboro, MA, UNITED STATES

Shankara, Srinivas, Shrewsbury, MA, UNITED STATES

NUMBER KIND DATE US 2002006397 A1 20020117 US 2001-843342 A1 20010425 PATENT INFORMATION: APPLICATION INFO.: A1 20010425 (9)

NUMBER DATE

PRIORITY INFORMATION: US 2000-200562P 20000428 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: GENZYME CORPORATION, LEGAL DEPARTMENT, 15 PLEASANT ST

CONNECTOR, FRAMINGHAM, MA, 01701-9322

NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
2349

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 17 OF 20 USPATFULL on STN

ACCESSION NUMBER: 2001:235097 USPATFULL

Fungal antigens and process for producing the same TITLE:

Takesako, Kazutoh, Otsu, Japan INVENTOR(S):

Mizutani, Shigetoshi, Gamo-gun, Japan Endo, Masahiro, Kusatsu, Japan

Kato, Ikunoshin, Uji, Japan

PATENT ASSIGNEE(S): Takara Shuzo Co., Ltd., Kyoto, Japan (non-U.S.

corporation)

NUMBER KIND DATE _______ US 6333164 B1 20011225 US 1999-262856 19990304 (9) PATENT INFORMATION: APPLICATION INFO.:

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 1997-JP3041, filed

on 29 Aug 1997

NUMBER DATE ______ PRIORITY INFORMATION: JP 1996-255400 19960904 JP 1997-99775 19970331

DOCUMENT TYPE: Utility DOCUMENT TYPE: UTILITY
FILE SEGMENT: GRANTED
FRIMARY EXAMINER: Smith, Lynette R. F.
ASSISTANT EXAMINER: Baskar, Padma

LEGAL REPRESENTATIVE: Birch, Stewart, Kolasch & Birch, LLP

NUMBER OF CLAIMS: 12 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 9 Drawing Figure(s); 9 Drawing Page(s)

LINE COUNT: 2782

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 18 OF 20 USPATFULL on STN

ACCESSION NUMBER: 2001:67794 USPATFULL

TITLE: Human respiratory syncytial virus peptides with

antifusogenic and antiviral activities

Barney, Shawn O'Lin, Cary, NC, United States INVENTOR(S):

Lambert, Dennis Michael, Cary, NC, United States Petteway, Stephen Robert, Cary, NC, United States

Trimeris, Inc., Durham, NC, United States (U.S. PATENT ASSIGNEE(S):

corporation)

NUMBER KIND DATE _______ US 6228983 PATENT INFORMATION: B1 20010508 US 1995-485264 19950607 APPLICATION INFO .: (8)

Division of Ser. No. US 1995-470896, filed on 6 Jun RELATED APPLN. INFO.:

1995 Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994

Continuation-in-part of Ser. No. US 1993-73028, filed

on 7 Jun 1993, now patented, Pat. No. US 5464933

DOCUMENT TYPE:

Utility Granted FILE SEGMENT:

Scheiner, Laurie PRIMARY EXAMINER: ASSISTANT EXAMINER: Parkin, Jeffrey S. Pennie & Edmonds LLP LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: 62 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS:

84 Drawing Figure(s); 83 Drawing Page(s)

LINE COUNT: 32166

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 19 OF 20 EUROPATFULL COPYRIGHT 2003 WILA on STN

PATENT APPLICATION - PATENTANMELDUNG - DEMANDE DE BREVET

ACCESSION NUMBER: 1074617 EUROPATFULL EW 200106 FS OS

Primers for synthesising full-length cDNA and their use. TITLE:

Primers fuer Synthese von ganzen-Laenge cDNS und deren Anwendung.

Primers for synthesising full-length cDNA and their use. Ota, Toshio, 1-2-7-105, Tsujido Shinmachi, Fujisawa-shi, INVENTOR(S):

Kanagawa 251-0042, JP;

Isogai, Takao, 511-12, Ohmuro, Ami-machi, Inashiki-gun,

Ibaraki 300-0303, JP;

Nishikawa, Tetsuo, 27-3-403, Hikawa-cho, Itabashi-ku,

Tokyo 173-0013, JP;

Hayashi, Kohji, 1-9-446, Yushudai Nishi, Ichihara-shi,

Chiba 292-0056, JP;

Saito, Kaoru, 2-8-1-201, Kisarazu, Kisarazu-shi, Chiba

292-0056, JP;

Yamamoto, Junichi, 3-28-3-A101, Kiyomidai Higashi,

Kisarazu-shi, Chiba 292-0041, JP;

Ishii, Shizuko, 4508-19-202, Yana, Kisarazu-shi, Chiba

292-0812, JP;

Sugiyama, Tomoyasu, 2-6-23-102, Kiyomidai, Kisarazu-shi,

Chiba 292-0045, JP;

Wakamatsu, Ai, 1473-4-202, Takayanagi, Kisarazu-shi,

Chiba 292-0014, JP;

Nagai, Keiichi, 3-44-14-9-204, Sakuragaoka,

Higashiyamato-shi, Tokyo 207-0022, JP;

Otsuki, Tetsuji, 3-1-10-B102, Asahi, Kisarazu-shi, Chiba

292-0045, JP

Helix Research Institute, 1532-3 Yana, Kisarazu-shi, PATENT ASSIGNEE(S):

Chiba 292-0812, JP

PATENT ASSIGNEE NO: 2656450

AGENT: VOSSIUS & PARTNER, Siebertstrasse 4, 81675 Muenchen, DE

AGENT NUMBER: 100314 OTHER SOURCE: BEPA2001012 EP 1074617 A2 0253

Wila-EPZ-2001-H06-T1a SOURCE:

DOCUMENT TYPE: Patent

Anmeldung in Englisch; Veroeffentlichung in Englisch LANGUAGE: R AT; R BE; R CH; R CY; R DE; R DK; R ES; R FI; R FR; R DESIGNATED STATES:

GB; R GR; R IE; R IT; R LI; R LU; R MC; R NL; R PT; R

SE; R AL; R LT; R LV; R MK; R RO; R SI

PATENT INFO. PUB. TYPE: EPA2 EUROPAEISCHE PATENTANMELDUNG

PATENT INFORMATION:

PATENT NO KIND DATE ______ EP 1074617 A2 20010207 'OFFENLEGUNGS' DATE: 20010207 APPLICATION INFO.: EP 2000-116126 20000728 PRIORITY APPLN. INFO.: JP 1999-248036 19990729 JP 1999-300253 19990827 JP 2000-2000118776 20000111 JP 2000-2000183767 20000502 JP 2000-2000241899 20000609

ANSWER 20 OF 20 EUROPATFULL COPYRIGHT 2003 WILA on STN L4

PATENT APPLICATION - PATENTANMELDUNG - DEMANDE DE BREVET

EUROPATFULL EW 200002 FS OS ACCESSION NUMBER: 970966

FUNGAL ANTIGENS AND PROCESS FOR PRODUCING THE SAME. TITLE: PILZLICHE ANTIGENE UND VERFAHREN ZU DEREN HERSTELLUNG.

ANTIGENES FONGIOUES ET PROCESSUS DE FABRICATION.

TAKESAKO, Kazutoh, 4-20-208, Akibadai, Otsu-shi, Shiqa INVENTOR(S):

520, JP;

MIZUTANI, Shigetoshi, 1-86, Miyazu, Azuchi-cho, Gamo-gun, Shiga 521-13, JP;

ENDO, Masahiro, Hamoparesu-Kusatsu 405, 12-1, Nishishibukawa 2-chome, Kusatsu-shi, Shiga 525, JP; KATO, Ikunoshin, 1-1-150, Nanryo-cho, Uji-shi, Kyoto

611, JP

TAKARA SHUZO CO. LTD., 609 Takenaka-cho Fushimi-ku, PATENT ASSIGNEE(S):

Kyoto-shi, Kyoto 612, JP

PATENT ASSIGNEE NO: 710324

VOSSIUS & PARTNER, Siebertstrasse 4, 81675 Muenchen, DE AGENT:

AGENT NUMBER: 100314

100314 BEPA2000003 EP 0970966 A1 0048 Wila-EPZ-2000-H02-Tla OTHER SOURCE:

SOURCE:

DOCUMENT TYPE: Patent

LANGUAGE: Anmeldung in Japanisch; Veroeffentlichung in Englisch;

Verfahren in Englisch

DESIGNATED STATES: R DE; R FR; R GB; R IT; R NL

PATENT INFO.PUB.TYPE: EPA1 EUROPAEISCHE PATENTANMELDUNG (Internationale

Anmeldung)

PATENT INFORMATION:

PATENT NO KIND DATE ______ EP 970966 A1 20000112 L4 ANSWER 18 OF 20 USPATFULL on STN

INVENTOR(S):

ACCESSION NUMBER: 2001:67794 USPATFULL

Human respiratory syncytial virus peptides with TITLE:

antifusogenic and antiviral activities

Barney, Shawn O'Lin, Cary, NC, United States Lambert, Dennis Michael, Cary, NC, United States

Petteway, Stephen Robert, Cary, NC, United States PATENT ASSIGNEE(S): Trimeris, Inc., Durham, NC, United States (U.S.

corporation)

NUMBER KIND DATE -----US 6228983 B1 20010508 US 1995-485264 19950607 PATENT INFORMATION:

APPLICATION INFO.: 19950607 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 Continuation-in-part of Ser. No. US 1994-360107,

filed on 20 Dec 1994 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994

Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

DOCUMENT TYPE: Utility Granted FILE SEGMENT:

PRIMARY EXAMINER: Scheiner, Laurie
ASSISTANT EXAMINER: Parkin, Jeffrey Parkin, Jeffrey S. LEGAL REPRESENTATIVE: Pennie & Edmonds LLP

62 NUMBER OF CLAIMS:

EXEMPLARY CLAIM: NUMBER OF DRAWINGS: 84 Drawing Figure(s); 83 Drawing Page(s)

LINE COUNT: 32166

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 20 OF 20 EUROPATFULL COPYRIGHT 2003 WILA on STN L4

PATENT APPLICATION - PATENTANMELDUNG - DEMANDE DE BREVET

970966 EUROPATFULL EW 200002 FS OS ACCESSION NUMBER:

FUNGAL ANTIGENS AND PROCESS FOR PRODUCING THE SAME. TITLE: PILZLICHE ANTIGENE UND VERFAHREN ZU DEREN HERSTELLUNG.

ANTIGENES FONGIQUES ET PROCESSUS DE FABRICATION.

TAKESAKO, Kazutoh, 4-20-208, Akibadai, Otsu-shi, Shiga INVENTOR(S):

MIZUTANI, Shigetoshi, 1-86, Miyazu, Azuchi-cho,

Gamo-gun, Shiga 521-13, JP;

ENDO, Masahiro, Hamoparesu-Kusatsu 405, 12-1, Nishishibukawa 2-chome, Kusatsu-shi, Shiga 525, JP; KATO, Ikunoshin, 1-1-150, Nanryo-cho, Uji-shi, Kyoto

611. JP

TAKARA SHUZO CO. LTD., 609 Takenaka-cho Fushimi-ku, PATENT ASSIGNEE(S):

Kyoto-shi, Kyoto 612, JP

PATENT ASSIGNEE NO: 710324

VOSSIUS & PARTNER, Siebertstrasse 4, 81675 Muenchen, DE AGENT:

AGENT NUMBER: 100314

BEPA2000003 EP 0970966 A1 0048 OTHER SOURCE:

Wila-EPZ-2000-H02-T1a SOURCE:

DOCUMENT TYPE: Patent

LANGUAGE: Anmeldung in Japanisch; Veroeffentlichung in Englisch;

Verfahren in Englisch

DESIGNATED STATES: R DE; R FR; R GB; R IT; R NL

PATENT INFO.PUB.TYPE: EPA1 EUROPAEISCHE PATENTANMELDUNG (Internationale

Anmeldung)

PATENT INFORMATION: PATENT NO KIND DATE

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EP 970966
                                          A1 20000112
'OFFENLEGUNGS' DATE:
                                              20000112
APPLICATION INFO.:
                     EP 1997-937856
                                              19970829
PRIORITY APPLN. INFO.: JP 1996-255400
                                              19960904
                      JP 1997-99775
                                              19970331
                      WO 97-JP3041
RELATED DOC. INFO .:
                                          970829 INTAKZ
                      WO 9809990
                                         980312 INTPNR
DETDEN. . . activity for releasing cytokines, such as IFN-.gamma. from the
       cells. The cytokine-releasing cells include, for example, T lymphocytes,
       natural killer (NK) cells, and the like. On the
       other hand, the present inventors have clarified that the insoluble
       fraction obtainable from protoplasts derived. . .
       The results are shown in Table 1. The insoluble fraction Ca-LSP
       exhibited more potent vaccine activity than the ribosome fraction (
       HSP) and the soluble fraction (HSS). <image>
           2) Comparison of vaccine activity of Candida albicans insoluble
       fraction Ca-LSP with living cell vaccine: The. . .
=> d history
     (FILE 'HOME' ENTERED AT 16:53:38 ON 14 SEP 2003)
     FILE 'MEDLINE, BIOSIS, SCISEARCH, CANCERLIT, LIFESCI, BIOTECHDS, CAPLUS'
     ENTERED AT 16:54:13 ON 14 SEP 2003
     FILE 'PCTFULL, USPATFULL, EUROPATFULL' ENTERED AT 17:24:17 ON 14 SEP 2003
L1
          11572 S (NK OR (NATURAL(W)KILLER)) (W) CELL#
         14866 S HEAT (W) SHOCK (W) PROTEIN# OR HSP###
L2
L3
           126 S SOLUBLE (5A) L2
            20 S L1 AND L3
L4
\Rightarrow s soluble(4a)12
          110 SOLUBLE (4A) L2
=> s soluble(4W)12
           80 SOLUBLE (4W) L2
=> s 16/t,ab
'T' IS NOT A VALID FIELD CODE
'T' IS NOT A VALID FIELD CODE
'T' IS NOT A VALID FIELD CODE
            0 L6/T,AB
=> s 16/ti,ab
            0 L6/TI.AB
=> s 12/ti,ab
          576 L2/TI.AB
=> s 19 and 11
           52 L9 AND L1
T.10
=> s 110 and pd<19990329
L11
            4 L10 AND PD<19990329
=> d ibib tot
      ANSWER 1 OF 4
                        PCTFULL COPYRIGHT 2003 Univentio on STN
ACCESSION NUMBER:
                        1998050424 PCTFULL ED 20020514
TITLE (ENGLISH):
                       HUMAN SERINE PROTEASE PRECURSOR
TITLE (FRENCH):
                      PRECURSEUR DE SERINE PROTEASE HUMAINE
                       HILLMAN, Jennifer, L.;
INVENTOR(S):
```

CORLEY, Neil, C.;

SHAH, Purvi

PATENT ASSIGNEE(S): INCYTE PHARMACEUTICALS, INC.;

HILLMAN, Jennifer, L.;

CORLEY, Neil, C.;

SHAH, Purvi LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE

_____ A2 19981112 WO 9850424

DESIGNATED STATES

AT AU BR CA CH CN DE DK ES FI GB IL JP KR MX NO NZ RU SE SG US GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

WO 1998-US9096 A 19980506 APPLICATION INFO.: US 1997-08/851,974 19970507 PRIORITY INFO.:

TITLE (FRENCH):

LANGUAGE OF PUBL.:

DOCUMENT TYPE: PATENT INFORMATION:

L11 ANSWER 2 OF 4 PCTFULL COPYRIGHT Z003 CHILL 1998031803 PCTFULL ED 20020514
THERAPIES INVOLVING MUTATED HEAT SHOCK TRANSCRIPTION TRAITEMENTS COMPRENANT UN FACTEUR DE TRANSCRIPTION DE

INVENTOR(S):

INVENTOR(S):

PATENT ASSIGNEE(S):

CHOC THERMIQUE MUTE

VOELLMY, Richard, W.

THE UNIVERSITY OF MIAMI;

VOELLMY, Richard, W.

VOELLMY, Richard, W. English Patent

NUMBER

KIND DATE _____

WO 9831803 A1 19980723

DESIGNATED STATES

w·

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

WO 1998-US1038 A 19980121

US 1997-60/035,662 19970121 US 1997-8/914,646 19970819

APPLICATION INFO.:

PRIORITY INFO.:

INVENTOR(S):

PATENT ASSIGNEE(S): FORDHAM UNIVERSITY LANGUAGE OF PUBL.:

DOCUMENT TYPE: PATENT INFORMATION:

L11 ANSWER 3 OF 4 PCTFULL COPYRIGHT 2003 UNITED ACCESSION NUMBER: 1998015616 PCTFULL ED 20020514
METHODS FOR GENERATING CYTOTOXIC T CELLS IN VITRO CEMPERATION IN VITRO DE LYMPHOCYTES T CYTOTOXIQUES

SRIVASTAVA, Pramod, K.;

BINDER, Robert; BLACHERE, Nathalie, E.

English

Patent

NUMBER ______

KIND DATE

WO 9815616 A1 19980416

DESIGNATED STATES

AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE GH HU ID W: IL IS JP KG KP KR KZ LC LK LR LT LV MD MG MK MN MX NO

NZ PL RO RU SG SI SK SL TJ TM TR TT UA UZ VN YU GH KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH

DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1997-US18110 A 19971006 PRIORITY INFO.: US 1996-8/726,967 19961007

L11 ANSWER 4 OF 4 USPATFULL on STN

ACCESSION NUMBER: 1999:4419 USPATFULL

Human serine protease precursor TITLE:

Hillman, Jennifer L., San Jose, CA, United States INVENTOR(S): Corley, Neil C., Mountain View, CA, United States

Shah, Purvi, Sunnyvale, CA, United States

PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., Palo Alto, CA, United

States (U.S. corporation)

NUMBER KIND DATE ______

US 5858758 PATENT INFORMATION: 19990112 <--

19970507 (8) US 1997-851974 APPLICATION INFO.:

DOCUMENT TYPE: Utility FILE SEGMENT: Granted PRIMARY EXAMINER: Wax, Robert A.

ASSISTANT EXAMINER: Moore, William W.

LEGAL REPRESENTATIVE: Mohan-Peterson, Sheela, Billings, Lucy J.Incyte

Pharmaceuticals, Inc.

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)

LINE COUNT: 1963

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d ibib kwic 2 3 4

ANSWER 2 OF 4 PCTFULL COPYRIGHT 2003 Univentio on STN T.11

1998031803 PCTFULL ED 20020514 ACCESSION NUMBER:

TITLE (ENGLISH): THERAPIES INVOLVING MUTATED HEAT SHOCK TRANSCRIPTION

FACTOR

TRAITEMENTS COMPRENANT UN FACTEUR DE TRANSCRIPTION DE TITLE (FRENCH):

CHOC THERMIQUE MUTE

VOELLMY, Richard, W. INVENTOR(S):

PATENT ASSIGNEE(S): THE UNIVERSITY OF MIAMI; VOELLMY, Richard, W.

LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION:

NUMBER KIND DATE

WO 9831803 A1 19980723

DESIGNATED STATES

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE W: ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU

SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ

CF CG CI CM GA GN ML MR NE SN TD TG WO 1998-US1038 A 19980121

APPLICATION INFO .: US 1997-60/035,662 19970121 PRIORITY INFO.:

US 1997-8/914,646 19970819

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A1 19980723
PΙ
      WO 9831803
```

The present invention relates to exogenous mutant HSF (mutHSF encoded by ABEN exogenous DNA) alters

expression or synthesis of endogenous heat shock protein (hsp) genes in eukaryotic cells, tissues

and organisms (e.g., mammalian, particularly human, cells, tissues and organisms). As described

herein, mutHSF has been shown to regulate expression of endogenous hsp in cells and, as a result, to

alter the response of the cells to stress. The mutHSF of the present. .

ABFR . . . mutant exogene

(mutHSF code par un ADN exogene) alterant l'expression ou la synthese de genes d'une proteine de

choc thermique (hsp) endogene dans des cellules, des tissus et des organismes eucaryotes (par

exemple des cellules, des tissus et des organismes de mammiferes et notamment, d'humains). Dans le

procede selon l'invention, mutHSF regule l'expression d'une hsp endogene dans des cellules, et,

ensuite, altere la reponse des cellules au stress. Le mutHSF de la presente invention est. .

DETD . . . with anti-hsp70

antibody blockade, Multhoff et al. were able to correlate hsp70 surface expression on certain cell lines with increased sensitivity to IL2-stimulated CD3-

natural killer cells. Note that in this as

other studies claiming hsp70 surface expression all that was shown was anti-hsp7o antibody recognition of.

L11 ANSWER 3 OF 4 PCTFULL COPYRIGH: 2000 1 1998015616 PCTFULL ED 20020514

ACCESSION NUMBER: 1998015616 PCTFULL ED 20020514

METHODS FOR GENERATING CYTOTOXIC T CELLS IN VITRO DE LYMPHOCYTES T

SRIVASTAVA, Pramod, K.; INVENTOR(S):

BINDER, Robert;

BLACHERE, Nathalie, E. PATENT ASSIGNEE(S): FORDHAM UNIVERSITY

LANGUAGE OF PUBL.: English Patent

DOCUMENT TYPE:

PATENT INFORMATION:

NUMBER KIND DATE

WO 9815616 A1 19980416

DESIGNATED STATES

AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE GH HU ID W: IL IS JP KG KP KR KZ LC LK LR LT LV MD MG MK MN MX NO

NZ PL RO RU SG SI SK SL TJ TM TR TT UA UZ VN YU GH KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH

DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG

CI CM GA GN ML MR NE SN TD TG

WO 1997-US18110 A 19971006 US 1996-8/726,967 19961007 APPLICATION INFO .: PRIORITY INFO.:

A1 19980416 WO 9815616 ABEN . . into

antigen-reactive cytotoxic T cells. The effectiveness of the procedure may be enhanced by repeated

restimulations and/or the addition of heat shock protein-peptide complexes. Methods and compositions

are also disclosed for the treatment and prevention in a subject of

cancer or infectious disease. . .

DETD . . . system arise from pluripotent stem
20 cells through two main lines of differentiation: a) the
lymphoid lineage producing lymphocytes (T cells, B cells,
natural killer cells), and b) the myeloid
lineage (monocytes,
macrophages and neutrophils) and other accessory cells
(dendrizic cells, platelets and mast cells). In the

25 circulatory. . .

L11 ANSWER 4 OF 4 USPATFULL on STN

ACCESSION NUMBER: 1999:4419 USPATFULL

TITLE: Human serine protease precursor

INVENTOR(S): Hillman, Jennifer L., San Jose, CA, United States
Corley, Neil C., Mountain View, CA, United States

Shah, Purvi, Sunnyvale, CA, United States

PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., Palo Alto, CA, United

States (U.S. corporation)

PATENT INFORMATION: US 5858758 19990112 <-APPLICATION INFO.: US 1997-851974 19970507 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY FYAMINER: Wax. Robert A

PRIMARY EXAMINER: Wax, Robert A.
ASSISTANT EXAMINER: Moore, William W.

LEGAL REPRESENTATIVE: Mohan-Peterson, Sheela, Billings, Lucy J.Incyte

Pharmaceuticals, Inc.

NUMBER OF CLAIMS: 8 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)

LINE COUNT: 1963

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5858758 19990112 <--

AB The present invention provides a human serine protease precursor (
HSPP) and polynucleotides which encode HSPP. The
invention also provides expression vectors, host cells, agonists,
antisense molecules, antibodies, or antagonists. The invention also
provides methods for treating disorders associated with expression of
HSPP.

SUMM A series of six SP have been identified in murine cytotoxic T-lymphocytes (CTL) and natural killer (NT) cells.

These SP are involved with CTL and NK cells in the destruction of virally transformed cells and tumor cells and in organ and tissue transplant rejection (Zunino, S. J.. . .

DRWD FIGS. 2A and 2B show the amino acid sequence alignments between HSPP (SEQ ID NO:1), the rat natural killer cell protease-1 precursor, RNKP-1 (GI 206690; SEQ ID NO:3), and a human serine esterase from cytotoxic T lymphocytes, SECT (GI 306682; . .

=> d history

L1

(FILE 'HOME' ENTERED AT 16:53:38 ON 14 SEP 2003)

FILE 'MEDLINE, BIOSIS, SCISEARCH, CANCERLIT, LIFESCI, BIOTECHDS, CAPLUS' ENTERED AT 16:54:13 ON 14 SEP 2003

FILE 'PCTFULL, USPATFULL, EUROPATFULL' ENTERED AT 17:24:17 ON 14 SEP 2003 11572 S (NK OR (NATURAL(W)KILLER))(W)CELL#

L2 14866 S HEAT (W) SHOCK (W) PROTEIN# OR HSP###

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126 S SOLUBLE (5A) L2
L3
            20 S L1 AND L3
L4
           110 S SOLUBLE (4A) L2
L5
           80 S SOLUBLE (4W) L2
L6
L7
            0 S L6/T,AB
0 S L6/TI,AB
L8
           576 S L2/TI,AB
T.9
L10
            52 S L9 AND L1
L11
              4 S L10 AND PD<19990329
=> s 11/ti,ab
          293 L1/TI,AB
L12
=> s 112 and 15
         2 L12 AND L5
=> d ibib tot
                        PCTFULL COPYRIGHT 2003 Univentio on STN
       ANSWER 1 OF 2
ACCESSION NUMBER: 2003068822 PCTFULL ED 2003068822 PCTFULL

DE-IMMUNIZED (POLY) PEPTIDE CONSTRUCTS

DE-IMMUNIZED (POLY) PEPTIDIOUES DESIM
                        2003068822 PCTFULL ED 20030903 EW 200334
                        CONSTRUCTIONS (POLY) PEPTIDIQUES DESIMMUNISEES
                         ZOCHER, Marcel, Friedrich-Heckerstr. 34, D-79539
INVENTOR(S):
                         Loerrach, DE [DE, DE];
                         DREIER, Torsten, Johann-Clanze-Strasse 39, D-81369
                         Muenchen, DE [DE, DE];
                         BAeUERLE, Patrick, Waldpromenade 18C, D-82131 Gauting,
                         DE [DE, DE]
                         MICROMET AG, Staffelseestrasse 2, D-81477 Muenchen, DE
PATENT ASSIGNEE(S):
                         [DE, DE], for all designates States except US;
                         ZOCHER, Marcel, Friedrich-Heckerstr. 34, D-79539
                         Loerrach, DE [DE, DE], for US only;
                         DREIER, Torsten, Johann-Clanze-Strasse 39, D-81369 Muenchen, DE [DE, DE], for US only;
                         BAeUERLE, Patrick, Waldpromenade 18C, D-82131 Gauting,
                         DE [DE, DE], for US only
                         VOSSIUS & PARTNER$, Siebertsrasse 4, D-81765 Muenchen$,
AGENT:
                         DE
LANGUAGE OF FILING:
                         English
                         English
LANGUAGE OF PUBL.:
DOCUMENT TYPE:
                         Patent
PATENT INFORMATION:
                         NUMBER KIND DATE
                         _____
                         WO 2003068822 A2 20030821
DESIGNATED STATES
       W:
                         AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
                         CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
                         IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
                        MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG
                        SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
                        GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
       RW (ARIPO):
                        AM AZ BY KG KZ MD RU TJ TM
       RW (EAPO):
                        AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU
       RW (EPO):
                        MC NL PT SE SI SK TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG APPLICATION INFO.: WO 2003-EP1389 A 20030212
PRIORITY INFO.:
                       EP 2002-02003332.0
                                                 20020213
       ANSWER 2 OF 2
L13
                        PCTFULL COPYRIGHT 2003 Univentio on STN
ACCESSION NUMBER:
                        2002016414 PCTFULL ED 20020711 EW 200209
TITLE (ENGLISH):
                       COMPOSITION FOR THE ELIMINATION OF AUTOREACTIVE B-CELLS
                       COMPOSITION DESTINEE A L'ELIMINATION DES CELLULES B
TITLE (FRENCH):
```

AUTOREACTIVES

ZOCHER, Marcel, Theodor-Koerner-Str. 13, 82049 INVENTOR(S):

Muenchen-Pullach, DE [DE, DE];

BAeUERLE, Patrick, Vogelsangstr. 13A, 82152 Gauting, DE

[DE, DE];

DREIER, Torsten, Johann-Clanze-Str. 39, 81369 Muenchen,

DE [DE, DE]

MICROMET AG, Am Klopferspitz 19, 82152 PATENT ASSIGNEE(S):

Martinsried/Muenchen, DE [DE, DE], for all designates

States except US;

ZOCHER, Marcel, Theodor-Koerner-Str. 13, 82049

Muenchen-Pullach, DE [DE, DE], for US only;

BAeUERLE, Patrick, Vogelsangstr. 13A, 82152 Gauting, DE [DE, DE], for US only;

DREIER, Torsten, Johann-Clanze-Str. 39, 81369 Muenchen,

DE [DE, DE], for US only

VOSSIUS & PARTNER\$, Sieberstr. 4, 81675 Muenchen\$, DE

LANGUAGE OF FILING: LANGUAGE OF PUBL.: DOCUMENT TYPE:

AGENT:

1)

English English Patent

PATENT INFORMATION:

NUMBER KIND DATE ______

A2 20020228 WO 2002016414

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK

SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZW

AM AZ BY KG KZ MD RU TJ TM RW (EAPO):

AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE RW (EPO):

TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG APPLICATION INFO:: WO 2001-EP9714 A 20010822 PRIORITY INFO:: EP 2000-00117354.1 20000822

=> d history

(FILE 'HOME' ENTERED AT 16:53:38 ON 14 SEP 2003)

FILE 'MEDLINE, BIOSIS, SCISEARCH, CANCERLIT, LIFESCI, BIOTECHDS, CAPLUS' ENTERED AT 16:54:13 ON 14 SEP 2003

FILE 'PCTFULL, USPATFULL, EUROPATFULL' ENTERED AT 17:24:17 ON 14 SEP 2003

L111572 S (NK OR (NATURAL(W)KILLER))(W)CELL#

L214866 S HEAT (W) SHOCK (W) PROTEIN# OR HSP###

126 S SOLUBLE (5A) L2 L3

20 S L1 AND L3 L4

110 S SOLUBLE (4A) L2 L5

80 S SOLUBLE (4W) L2 L6

0 S L6/T,AB L7

L8 0 S L6/TI,AB

L9 576 S L2/TI.AB

52 S L9 AND L1 L10

L11 4 S L10 AND PD<19990329

293 S L1/TI,AB L12

L13 2 S L12 AND L5

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COST IN U.S. DOLLARS

SINCE FILE TOTAL

ENTRY SESSION 62.16 104.84

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 17:41:25 ON 14 SEP 2003

FULL ESTIMATED COST

L11 ANSWER 7 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1998:296438 BIOSIS DOCUMENT NUMBER: PREV199800296438

TITLE: The role of heat shock proteins in the stimulation of an

immune response.

AUTHOR(S): Multhoff, Gabriele (1); Botzler, Claus; Issels, Rolf CORPORATE SOURCE: (1) GSF-Inst. Clin. Hematol., Marchioninistr. 25, D-81377

(1) GSF-Inst. Clin. Hematol., Marchioninistr. 25, D-8. Munich Germany

Biological Chemistry, (March, 1998) Vol. 379, No.

3, pp. 295-300. ISSN: 1431-6730.

DOCUMENT TYPE: General Review

LANGUAGE: English

AB Heat shock proteins (HSP) have been defined as immunodominant, although most of them are highly conserved and ubiquitously distributed. Members

οf

SOURCE:

the 60, 70 and 90 kDa HSP families are involved in important aspects of viral and bacterial infections, in autoimmune diseases and in cancer immunity. HSP act as immunological target structures either by themselves because of an unusual expression pattern, or they are carrier proteins

for

immunogenic peptides. In addition to a classical major histocompatibility complex (MHC) restricted T cell response, a major contribution in the recognition of heat shock proteins has been shown for non-MHC restricted effector cells including gamma/delta TcR positive T lymphocytes and natural killer (NK) cells.

DUPLICATE 15 ANSWER 22 OF 24 MEDLINE

91318159 MEDLINE ACCESSION NUMBER:

PubMed ID: 1861074 91318159 DOCUMENT NUMBER:

Natural killer cell clones TITLE:

can efficiently process and present protein antigens. Roncarolo M G; Bigler M; Haanen J B; Yssel H; Bacchetta R;

AUTHOR: de Vries J E; Spits H

DNAX Research Institute, Human Immunology Department, Palo CORPORATE SOURCE:

Alto, CA 94304-1104.

JOURNAL OF IMMUNOLOGY, (1991 Aug 1) 147 (3) SOURCE:

781-7.

Journal code: 2985117R. ISSN: 0022-1767.

United States PUB. COUNTRY:

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

Abridged Index Medicus Journals; Priority Journals FILE SEGMENT:

199108 ENTRY MONTH:

Entered STN: 19910922 ENTRY DATE:

Last Updated on STN: 19910922 Entered Medline: 19910830

NK cell clones obtained from three different donors AΒ

were tested for their ability to present soluble proteins to Ag-specific т

cell clones. All NK clones were CD2+CD3-CD56+, whereas the expression of

CD16 varied from clone to clone. The NK cell clones

were able to process and present tetanus toxoid (TT) to TT-specific T

cell

clones in a class II HLA restricted manner. The capacity of NK cell clones to function as APC was also observed using the house dust mite allergen Der p I and the Der p I-derived peptide Val89-Cys117. As with EBV-transformed B cell line, NK cell clones

could present the peptide 3-13 derived from the 65-kDa heat

shock protein of Mycobacterium leprae, but they were

unable to present the whole M. leprae Ag. Freshly isolated NK cells, IL-2-activated NK cells, and

NK cell lines expanded in vitro could also process and present TT. The ability of the different NK populations to act as

accessory cells correlated with their levels of class II HLA expression.

These data demonstrate that NK cell clones can

efficiently function as APC, however they may be restricted in the types of Ag that they can process.

6 ANSWER 21 OF 24 MEDLINE DUPLICATE 14

ACCESSION NUMBER: 93352110 MEDLINE

DOCUMENT NUMBER: 93352110 PubMed ID: 8349312

TITLE: Changes in the level of perforin and its transcript during

effector and target cell interactions.

AUTHOR: Kim K K; Blakely A; Zhou Z; Davis J; Clark W; Kwon B S
CORPORATE SOURCE: Department of Microbiology and Immunology, Indiana

University School of Medicine, Indianapolis 46202.

CONTRACT NUMBER: DE10525 (NIDCR)

K11DE00310 (NIDCR) MAI-28175 (NIAID)

SOURCE: IMMUNOLOGY LETTERS, (1993 May) 36 (2) 161-9.

Journal code: 7910006. ISSN: 0165-2478.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199309

ENTRY DATE: Entered STN: 19931001

Last Updated on STN: 20000303 Entered Medline: 19930915

AB Perforin is a cytoplasmic granule protein expressed in cytotoxic lymphocytes, and is capable of lysing target cells. This protein is induced as cytotoxic T cells are activated, and the mRNA

 $\mbox{\ \ expression is modulated by various stimulators. These observations suggest$

possible changes in the level of perforin transcripts and protein when killer lymphocytes meet specific target cells leading to target cell death. To address this question, we examined three murine T-cell clones and primary human NK cells in perforin expression.

When the cytotoxic lymphocytes were exposed to sensitive targets, perforin

mRNA disappeared within 5 to 30 min and appeared within an hour thereafter. Among the murine T cell clones, L3 and OE4 showed two phases of mRNA decrease while human NK cells and the third

murine T cell clone, AB.1, showed only one phase of mRNA loss during a $240\,$

min period. The data indicate that when cytotoxic lymphocytes receive signals from a sensitive target, the cells rapidly degrade previously accumulated perforin mRNA and synthesize new transcripts. Interestingly, heat shock protein 70 mRNA was induced as the perforin mRNA levels recovered, while P55 I1-2 receptor mRNA was downregulated within 5 min after exposure to targets. The perforin

protein

level also rapidly decreased immediately after the interaction with the target, followed by a recovery, and then another decrease as seen in primary human NK cells, OE4 and L3 cells. However, in

the AB.1 clone, no change in perforin content was detectable, despite the loss of perforin mRNA.(ABSTRACT TRUNCATED AT 250 WORDS)

ANSWER 18 OF 24 MEDLINE DUPLICATE 12

94044776 MEDITNE ACCESSION NUMBER:

94044776 PubMed ID: 8228242 DOCUMENT NUMBER:

70 kDa heat shock cognate protein is a transformation-TITLE:

associated antigen and a possible target for the host's

anti-tumor immunity.

Tamura Y; Tsuboi N; Sato N; Kikuchi K AUTHOR:

Department of Pathology, Sapporo Medical University School CORPORATE SOURCE:

of Medicine, Japan.

JOURNAL OF IMMUNOLOGY, (1993 Nov 15) 151 (10) SOURCE:

5516-24.

Journal code: 2985117R. ISSN: 0022-1767.

United States PUB. COUNTRY: Journal; Article; (JOURNAL ARTICLE) DOCUMENT TYPE:

English LANGUAGE: Abridged Index Medicus Journals; Priority Journals

FILE SEGMENT: 199312 ENTRY MONTH:

ENTRY DATE: Entered STN: 19940117

> Last Updated on STN: 19990129 Entered Medline: 19931210

We previously investigated a novel heat-inducible transformation-AΒ associated cell surface Aq that is expressed on the activated H-ras oncogene-transformed rat fibrosarcoma W31, but not its parental nontransformed fibroblast WFB. This Ag was detected by mAb 067. Herein,

we

characterized the molecular nature of the Ag by using anti-heat shock protein (HSP) mAb. The accumulated data indicated that the cell surface expression of Ag was clearly enhanced by several stressors, such as TNF, L-azetidine-2-carboxylic acid, and sodium arsenite. The immunoprecipitate made with mAb 067 and W31 cell lysates reacted with anti-rat 70 kDa heat shock cognate (HSC) mAb, TG5E, .indicating that 067-defined Ag may be a rat 70 kDa HSC. Because this Ag seemed to be one of the transformation-associated Ag of WFB, we further studied whether it could play an important role in the host's anti-tumor immunity. Peripheral T cells of rats primed with live BCG showed cytotoxicity to W31 but not to WFB. Because the possibility existed that HSP may interact with certain populations of T cells, we focused on the reactivity of CD4-CD8- double negative T (DNT) cells against 067-defined molecule. DNT cells from spleen and PBL of live BCG-primed rats showed the cytotoxicity against W31 cells. This cytotoxicity was completely blocked by mAb 067 and anti-CD3 mAb. However, it was not blocked by mAb R48B1 and 109, which detect the MHC class I nonpolymorphic determinant and a target molecule of the cytolysis by poly I:C-induced NK cells, respectively. Furthermore, brefeldin A was able to block the cytotoxicity against W31 targets by DNT cells, but not by NK cells. These data suggest that 70 kDa HSC may be a tumor Ag and may act as a presenting molecule perhaps complexed with cellular peptides to certain DNT cells.

L6 ANSWER 17 OF 24 CANCERLIT

ACCESSION NUMBER: 95607573 CANCERLIT

DOCUMENT NUMBER: 95607573

TITLE: Induction of non-mhc restricted killer cells: differential

induction of effector populations by tumour cell lines.

AUTHOR: Selin L K

CORPORATE SOURCE: Univ. of Manitoba, Canada.

SOURCE: Diss Abstr Int [B], (1994) 55 (3) 814.

ISSN: 0419-4217.

DOCUMENT TYPE: (THESIS)
LANGUAGE: English

FILE SEGMENT: Institute for Cell and Developmental Biology

ENTRY MONTH: 199506

ENTRY DATE: Entered STN: 19950608

Last Updated on STN: 19970509

The nonadaptive immune response characterized by non-MHC-restricted AB cytotoxic effectors appears to play a significant role in host cellular immunity against both infectious diseases and tumors. It is possible that cytotoxic responsiveness of these effectors to 'altered' tumor cells also implies a capacity to induce the effector population. A systematic examination of different tumor cell lines did demonstrate a differential ability of tumor cell lines to induce effectors both NK cells and gamma, delta T cells. The properties and characteristics which made tumor cell lines into effective inducers were examined as well as the nature of the effector populations. Lymphoblastoid B cell lines (LBL) were the most effective inducers of non-MHC restricted killer cell activity as they induced enhanced levels of cytotoxic activity and stimulated proliferative responses in the responder population. Different LBL alone or in conjunction with IL-2 were able to stimulate non-MHC restricted cytotoxic activity in NK cells, gamma, delta and alpha, beta T cells. The phenotype(s) which was induced was dependent on the specific LBL used in the induction system as well as the presence of IL-2. The presence of Epstein-Barr virus (EBV) infection was found to significantly enhance LBL cytotoxic and proliferation inductive capacity as well as the proportion of CD16+ cells. Studies using EBV+ and EBV- LBL suggested that at least two parameters were involved in the EBV+ LBL induction process, the presence of a stimulating antigen on the LBL which specifically stimulates CD16+ cells and a second element which results in the induction of IL-2. Neither parameter was sufficient alone. Consistent with the hypothesis that a LBL cell surface molecule was involved in the induction was the observations that cellular contact was found to be essential. As well antibodies to 3 classes of adhesion molecules (CD2, CD18, and CD29) were found to inhibit LBL induction of non-MHC restricted killer cell activity. Two LBL, RPMI 8226 and Daudi were found to be

potent

inducers of Vgamma9 expressing T cells. This inductive capacity was not a general property of LBL nor did it relate to the presence of EBV nor to the tumor type of the B cell line. RPMI 8226 induced a population of gamma, delta T cells which were heterogeneous in terms of their cell surface markers, patterns of proliferation and cytotoxic responses. A member of the groEL HSP family (HSP 58) has been suggested as the inducing molecule in Daudi cells. Although anti-HSP 58 was inhibitory to gamma, delta T cell induction by RPMI 8226, Daudi and mycobacterial products evidence is presented which suggests this may not be a specific effect. Collectively, the results suggest that some LBL cell surface stimulus can induce an activation and expansion of non-MHC restricted killer cells. In

the present studies the expansion of CD16+ and gamma,delta TCR+ effectors were examined. This inductive ability of LBL appears to relate in part to viral infection and in part to the phenotypic properties of the inducer. The nature of the stimulus is still unclear at this time but these results

do suggest that there is a clear distinction between target susceptibility $% \left(1\right) =\left(1\right) \left(1\right) +\left(1\right) \left(1\right) \left(1\right) +\left(1\right) \left(1$

and inductive capacity. (Abstract shortened by UMI.) (Full text available from University Microfilms International, Ann Arbor, MI, as Order No. AADNN-85917)

DUPLICATE 7 ANSWER 11 OF 24 MEDLINE

ACCESSION NUMBER: 96178427 MEDLINE

96178427 PubMed ID: 8598315 DOCUMENT NUMBER:

Noncytotoxic alkyl-lysophospholipid treatment increases TITLE:

sensitivity of leukemic K562 cells to lysis by natural

killer (NK) cells.

Erratum in: Int J Cancer 1996 May 29;66(5):713 COMMENT:

Botzler C; Kolb H J; Issels R D; Multhoff G AUTHOR:

GSF-Forschungszentrum fur Umwelt und Gesundheit GmbH, CORPORATE SOURCE: Institut fur Klinische Hamatologie, Munich, Germany.

INTERNATIONAL JOURNAL OF CANCER, (1996 Mar 1) 65 SOURCE:

(5) 633-8.

Journal code: 0042124. ISSN: 0020-7136.

United States PUB. COUNTRY:

Journal; Article; (JOURNAL ARTICLE) DOCUMENT TYPE:

LANGUAGE: English

Priority Journals FILE SEGMENT:

ENTRY MONTH: 199604

Entered STN: 19960506 ENTRY DATE:

> Last Updated on STN: 19980206 Entered Medline: 19960423

Alkyl-lysophospholipids (ALP) are a group of anti-cancer compounds that have previously been shown to have the unique feature of being

selectively

toxic to neoplastic tissues. Because alkyl-lysophospholipids target the cell membrane as their site of action, our aim was to analyse the immunological effects of a nonlethal ALP treatment on leukemic K562 cells.

In this in vitro study we used ET-18-OCH3, one of the most potent ALP derivatives, at different concentrations ranging from 25 up to 100 microgram/ml. By measurement of cell viability and of apoptosis, we determined a concentration of 25 microgram/ml ET-18-OCH3 and an incubation

period of 2 hr as nonlethal for K562 cells; higher concentrations

markedly reduced cell viability and led to induction of apoptosis. Similar to the effects induced by nonlethal heat shock, a nontoxic ET-18-OCH3 treatment led to a significant increase in the sensitivity of K562 cells to lysis

by

interleukin-2 (IL-2) stimulated natural killer (NK) cells. With respect to these results, we investigated the influence of nonlethal ALP treatment on the cell surface expression patterns and compared it to the results obtained with nonlethal heat shock. ALP treatment does not induce major histocompatibility complex (MHC) expression; however, a significant increase in the cell surface expression of HSP72 was shown by immunoblot analysis of membrane lysates of either untreated or ET-18-OCH3 treated K562 cells. The increased sensitivity of ET-18-OCH3 treated K562 cells to lysis by NK cells could be correlated with the elevated cell surface expression of HSP72.

L6 ANSWER 9 OF 24 MEDLINE DUPLICATE 5

ACCESSION NUMBER: 1998052205 MEDLINE

DOCUMENT NUMBER: 98052205 PubMed ID: 9392312

TITLE: Immunosuppression by D-isomers of HLA class I heavy chain

(amino acid 75 to 84)-derived peptides is independent of

binding to HSC70.

AUTHOR: Woo J; Iyer S; Cornejo M C; Gao L; Cuturi C; Soulillou J

P;

Buelow R

CORPORATE SOURCE: SangStat Medical Corporation, Menlo Park, California

94025,

USA.

SOURCE: TRANSPLANTATION, (1997 Nov 27) 64 (10) 1460-7.

Journal code: 0132144. ISSN: 0041-1337.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980116

Last Updated on STN: 19980116

Entered Medline: 19971230

BACKGROUND: Peptides derived from the class I heavy chain were shown to AB modulate immune responses in vitro and in vivo. A peptide derived from HLA-B2702 (2702.75-84) inhibited differentiation of cytotoxic T cells as well as T cell and natural killer cell -mediated cytotoxicity in vitro. Peptide-mediated immunomodulation seemed to be independent of the MHC proteins expressed by responder and stimulator cells. In vivo studies in rodents demonstrated prolongation of heart and skin allograft survival after peptide therapy. Here, the correlation between the peptide's biological activity and its amino acid sequence was analyzed using peptides derived from amino acid 75-84 of several mouse, rat, and human MHC class I proteins as well as peptides with single amino acid substitutions in the 2702.75-84 sequence. METHODS: Peptides consisting of both L- and D-amino acids were tested for inhibition of murine and human T cell-mediated and lymphokineactivated killer cell-mediated cytotoxicity, binding to hsc70, and prolongation of heart allograft survival in vivo. RESULTS: Replacement of glutamic acid residue (E) at position 75 with valine (V) resulted in a peptide [2702.75-84(E>V)] with increased in vitro and in vivo activity

but

unchanged affinity for hsc70. Surprisingly, both L- and D-isomers of 2702.75-84 and 2702.75-84(E>V) inhibited cytotoxic cells in vitro and prolonged heart allograft survival in vivo. However, as expected, the peptides consisting of D-amino acids did not bind to hsc70. CONCLUSION: Assuming that both D- and L-isomers modulate immune responses by similar mechanisms, these results suggest that the peptides' effect is

independent

of binding to hsc70.

L6 ANSWER 8 OF 24 MEDLINE DUPLICATE 4

ACCESSION NUMBER: 1999096156 MEDLINE

DOCUMENT NUMBER: 99096156 PubMed ID: 9881829

TITLE: Natural killer cell

reactivity: activation and cytolysis mechanism

models, involving heat shock

protein, haemopoietic histocompatibility, major histocompatibility complex and complement molecules.

AUTHOR: Manzo G

SOURCE: MEDICAL HYPOTHESES, (1998 Jul) 51 (1) 5-9. Ref:

30 Journal code: 7505668. ISSN: 0306-9877.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal: Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Space Life Sciences

ENTRY MONTH: 199903

to

the

ENTRY DATE: Entered STN: 19990402

Last Updated on STN: 19990402 Entered Medline: 19990322

AB The close association of heat shock protein

(HSP), haemopoietic histocompatibility (Hh), major

histocompatibility complex (MHC), and complement genes on the same chromosomal region, and the fact that all these genes are inherited on the

whole in each haplotype of an individual, might indicate some evolutionary

and functional correlations among them. Several data suggest for HSP70 molecules a possible role as a molecular target recognizable by natural killer (NK) cells. HSP70

sequences from both prokaryotic and eukaryotic organisms reveal that about $% \left(1\right) =\left(1\right) \left(1\right) +\left(1\right) \left(1\right) \left(1\right) +\left(1\right) \left(1$

half of the amino acid residues are identical and many of the remaining residues are similar. I here assume that NK reactivity might start, early in the immunogenesis process, as a effect of the interaction between HSP70 molecules and a hypothetical HSP receptor of yet immature non-cytolytic NK cells. To this receptor, an HSP molecule might act as an activator or an inhibitor depending on whether its amino acid residues are reactive or not with it, respectively. Later in the immunogenesis process, murine Hh or human equivalent molecules, dominantly expressed in bone marrow target cells, might select the non-reactive NK clones of an individual, inducing them

mature and express a lytic machinery. As a consequence of the NK maturation, proliferating hemopoietic target cells expressing only or mainly activator HSPs on their surface might undergo NK cytolysis. This might explain the NK lysis of apparently normal cells found in human foetal marrow; moreover, this might explain in some way

F1 hybrid resistance phenomenon. The NK reactivity of an individual would be further modulated by the expression on the NK surface of particular receptors (CD94, p58) specific for defined MHC molecules (Cw1, Cw3, Bw6, B7) on the target cells. Such a specific interaction would induce an 'NK

effector inhibition'. The NK reactivity mechanism might have been further evolutionarily modified and adapted by the involvement of other NK

receptors, such as CD11b (specific for the C3b factor of the complement) and CD16 (specific for the IgG Fc piece).Cooperation among HSP, MHC, CD11b, CD16, C3b and Fc allows us to propose original models of the activation and cytolysis mechanisms in the NK cytotoxicity and antibody-dependent cell cytotoxicity phenomena.

L6 ANSWER 4 OF 24 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 1999123776 MEDLINE

DOCUMENT NUMBER: 99123776 PubMed ID: 9924701
TITLE: Heat shock protein antibodies

in sarcoma patients undergoing 41.8 degrees C whole body

hyperthermia.

AUTHOR: Katschinski D M; Benndorf R; Wiedemann G J; Mulkerin D L;

Touhidi R; Robins H I

CORPORATE SOURCE: University of Wisconsin, School of Medicine, Madison,

USA.

SOURCE: JOURNAL OF IMMUNOTHERAPY, (1999 Jan) 22 (1)

67-70.

Journal code: 9706083. ISSN: 1524-9557.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)

(CLINICAL TRIAL, PHASE II)

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199903

ENTRY DATE: Entered STN: 19990402

Last Updated on STN: 19990402 Entered Medline: 19990325

AB Previous in vitro studies of sarcoma and normal cell lines exposed to 41.8

degrees C (x 60 min) demonstrated selective increased expression of

members of the **heat shock protein** (**HSP**) family 70 on the cell surface of the sarcoma cells only. One implication of these data relates to the clinical application of

targeting

a stress-inducible, tumor-specific immune response. We therefore elected to measure immune response parameters (i.e., serum antibodies against HSP701, 60, and 27) in six patients with sarcoma using a Western blot technique. These study patients received one to four successive 41.8 degrees C whole-body hyperthermia (WBH) x 60-min treatments (given every

3

weeks). We also tested the serum of 10 untreated healthy control subjects for the same parameters. In all patients, baseline HSP antibody levels were detectable; in no case did WBH result in an increase in HSP antibodies. The serum of one patient with sarcoma demonstrated a strong nonfluctuating reaction against HSP27 before and after WBH that had no obvious correlation; this was not observed in the sera of the control subjects. This study suggests that WBH does not induce a B-cell response to HSP family 70 antigens; these data, however, do not exclude the possibility of NK cell activation due to HSP antigen presentation.

L11 ANSWER 18 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

DOCUMENT NUMBER:

ACCESSION NUMBER: 1995:383492 BIOSIS PREV199598397792

TITLE:

A heat inducible heat shock

protein 72 (HSP72) associated

immunogenic determinant acts as a tumor specific recognition structure for NK cells.

AUTHOR(S):

Botzler, C.; Multhoff, G.; Wiesnet, M.; Wilmanns, W.;

Issels, R. D.

CORPORATE SOURCE:

GSF - Inst. Klin. Haematol., Munich Germany 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY.. (1995) pp. 488.

SOURCE: The 9th International Congress of Immunology.

Publisher: 9th International Congress of Immunology San

Francisco, California, USA.

Meeting Info.: Meeting, Sponsored by the American

Association of Immunologists and the International Union

of

Immunological Societies San Francisco, California, USA

July

23-29, 1995

DOCUMENT TYPE:

Conference

LANGUAGE: English L11 ANSWER 17 OF 20 MEDLINE DUPLICATE 9

ACCESSION NUMBER: 95359435 MEDLINE

DOCUMENT NUMBER: 95359435 PubMed ID: 7632945

TITLE: CD3- large granular lymphocytes recognize a heat-inducible

immunogenic determinant associated with the 72-kD heat

shock protein on human sarcoma cells.

AUTHOR: Multhoff G; Botzler C; Wiesnet M; Eissner G; Issels R CORPORATE SOURCE: GSF-Institut fur Klinische Hamatologie, Munchen, Germany.

SOURCE: BLOOD, (1995 Aug 15) 86 (4) 1374-82.

Journal code: 7603509. ISSN: 0006-4971.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199509

ENTRY DATE: Entered STN: 19950921

Last Updated on STN: 19970203 Entered Medline: 19950914

Traditionally, heat shock proteins (HSPs) are believed to be located intracellularly, where they perform a variety of chaperoning functions. Recently, evidence has accumulated that some tumor cells express HSPs on the cell surface. The present study confirms this finding and correlates HSP72 cell surface expression, induced by nonlethal heat shock, with an increased sensitivity to interleukin-2-stimulated CD3-natural killer (NK) cells. After nonlethal heat shock, a monoclonal antibody directed against the major heat-inducible 72-kD HSP (HSP72) stains the cell surface of sarcoma cells (ie, Ewing's sarcoma cells or osteosarcoma cells) but not that of normal cells (ie, peripheral blood lymphocytes, fibroblasts, phytohemagglutin-stimulated blasts, B-lymphoblastoid cell lines) or of mammary carcinoma cell line MX-1 carcinoma cells. In this study, we show for the first time a correlation of HSP72 cell surface expression with an increased susceptibility to lysis by NK effector cells. This finding is supported

by

the following points: (1) HLA-disparate effector cells show similar, elevated lysis of HSP72+ heat-treated sarcoma cells; (2) CD(3-) NK cells, but not CD3+ cytotoxic T lymphocytes, are responsible for the recognition of heat-shocked sarcoma cells; (3) by antibody-blocking studies, an immunogenic HSP72 determinant, which is expressed selectively on the cell surface of heat-treated sarcoma

cells could be correlated with NK recognition; (4) the reported phenomenon

is independent of a heat-induced, transient downregulation of major histocompatibility complex (MHC) class-I expression; and (5) blocking of MHC class-I-restricted recognition, using either MHC class-I-specific monoclonal antibody W6/32 on the target cells or alpha/beta T-cell receptor monoclonal antibody WT31 on effector cells, also has no inhibitory effect on the lysis of HSP72+ tumor cells. Finally, our in vitro data might have further clinical implications with respect

to

 ${\tt HSP72}$ as a stress-inducible, sarcoma-specific NK recognition structure.

L11 ANSWER 15 OF 20 MEDLINE DUPLICATE 8

ACCESSION NUMBER: 97157087 MEDLINE

DOCUMENT NUMBER: 97157087 PubMed ID: 9003468

TITLE: Heat-shock protein 72

cell-surface expression on human lung carcinoma cells in associated with an increased sensitivity to lysis mediated

by adherent natural killer

cells.

AUTHOR: Botzler C; Issels R; Multhoff G

CORPORATE SOURCE: GSF-National Research Centre for Environment and Health,

Institute of Clinical Hematology, Munich, Germany.

SOURCE: CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1996 Dec) 43

(4) 226-30.

Journal code: 8605732. ISSN: 0340-7004.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals ENTRY MONTH: 199702

ENTRY DATE: Entered STN: 19970305 Last Updated on STN: 19970305

Entered Medline: 19970219

AB The cell-surface expression patterns of major histocompatibility complex (MHC) class I, class II and heat-shock protein

72 (HSP72) molecules were measured on human lung (LX-1)

and mammary (MX-1) carcinoma cells. No major differences were found in

the

MHC cell-surface expression pattern of both cell lines. However, they differ significantly in their capacity to express HSP72 on their cell surface. Under physiological conditions LX-1 cells express HSP72 molecules on more than 90% of the cells, whereas MX-1 cells exhibit no significant HSP72 cell-surface expression (less than 5%). These expression patterns remained stable in all further cell passages tested. The sensitivity to lysis mediated by an interleukin-2 (IL-2)-stimulated, adherent natural killer (NK) cell population could be correlated with the amount of cell-surface-expressed HSP72 molecules. By antibody-blocking studies, using HSP72 -specific monoclonal antibody (mAb), a strong inhibition of lysis was

only

found with LX-1 cells but not with MX-1 cells. In contrast to the cell-surface expression, the cytoplasmic amount of ${\tt HSP72}$ in MX-1 cells was twice as high compared to LX-1 cells under physiological conditions. After nonlethal heat-shock the rate of induction and the

total

cytoplasmic amounts of HSP72 were comparable in both cell lines. The clonogenic cell viability of LX-1 cells after incubation at temperatures ranging from 41 degrees C to 44 degrees C was significantly elevated compared to that of MX-1 cells. In conclusion we state the following: (i) HSP72 cell-surface expression on human carcinoma cells is independent of the cytoplasmic amount of HSP72; (ii) the cell-surface expression of HSP72 is associated with an increased sensitivity of tumor cells to lysis mediated by an IL-2-stimulated, adherent NK cell population; (iii) thermoresistance is not related to the cytoplasmic HSP72 level but might be related to the amount of HSP72 expressed on the cell surface.

L11 ANSWER 14 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS

INC. DUPLICATE

7

1996:158870 BIOSIS ACCESSION NUMBER: PREV199698731005

DOCUMENT NUMBER:

Noncytotoxic alkyl-lysophospholipid treatment increases TITLE: sensitivity of leukemic K562 cells to lysis by natural

killer (NK) cells.

Botzler, Claus; Kolb, Hans-Jochem; Issels, Rolf D.; AUTHOR(S):

Multhoff, Gabriele

CORPORATE SOURCE: GSF-Inst. Klinische Haematologie, Marchioninistr. 25,

D-81377 Munich Germany

International Journal of Cancer, (1996) Vol. 65, No. 5, SOURCE:

pp.

. .

633-638.

ISSN: 0020-7136.

DOCUMENT TYPE:

Article

LANGUAGE:

English

Alkyl-lysophospholipids (ALP) are a group of anti-cancer compounds that have previously been shown to have the unique feature of being

toxic to neoplastic tissues. Because alkyl-lysophospholipids target the cell membrane as their site of action, our aim was to analyse the immunological effects of a nonlethal ALP treatment on leukemic K562

cells.

In this in vitro study we used ET-18-OCH-3, one of the most potent ALP derivatives, at different concentrations ranging from 25 up to 100 mu-g/ml. By measurement of cell viability and of apoptosis, we determined a concentration of 25 mu-g/ml ET-18-OCH-3 and an incubation period of 2

hr

as nonlethal for K562 cells; higher concentrations markedly reduced cell viability and led to induction of apoptosis. Similar to the effects induced by nonlethal heat shock, a nontoxic ET-18-OCH-3 treatment led to

significant increase in the sensitivity of K562 cells to lysis by interleukin-2 (IL-2) stimulated natural killer (NK) cells. With respect to these results, we investigated the influence of nonlethal ALP treatment on the cell surface expression patterns and compared it to the results obtained with nonlethal heat shock. ALP treatment does not induce major histocompatibility complex (MHC) expression; however, a significant increase in the cell surface expression of HSP72 was shown by immunoblot analysis of membrane lysates of either untreated or ET-18-OCH-3 treated K562 cells. The increased sensitivity of ET-18-OCH-3 treated K562 cells to lysis by NK cells could be correlated with the elevated cell surface expression of HSP72.

L11 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1997:128116 CAPLUS

DOCUMENT NUMBER: 126:169815

TITLE: Heat shock protein
72 (HSP72), a hyperthermia-inducible

immunogenic determinant on leukemic K562 and Ewing's

sarcoma cells

AUTHOR(S): Multhoff, G.

CORPORATE SOURCE: Inst. Klinische Haematologie, Munich, 81377, Germany

SOURCE: International Journal of Hyperthermia (1997)

), 13(1), 39-48

CODEN: IJHYEQ; ISSN: 0265-6736

PUBLISHER: Taylor & Francis

DOCUMENT TYPE: Journal LANGUAGE: English

AB Following non-lethal heat stress (41.cntdot.7.degree.C) and a recover period at 37.degree.Cm the inducible 72 kDa HSP (HSP72) is detectable selectively on the cell surface of human Ewing's Sarcoma (ES) and of leukemic K562 cells but not on EBV transformed B cells (B-LCL) which we generated from PBL of healthy human volunteers. The HSP72 expression was measured by flow-cytometric anal. using a monoclonal antibody (moAb) that specifically recognizes HSP72, the inducible form of the HSP70 group. The major histocompatibility complex (MHC) class I expression, detected with the moAb W6/32 was not affected by non-lethal heat exposure and a recovery period at 37 degree C for 12 b. FS cells express MHC class I mols, on

histocompatibility complex (MHC) class I expression, detected with the moAb W6/32 was not affected by non-lethal heat exposure and a recovery period at 37.degree.C for 12 h: ES cells express MHC class I mols. on about 80% of the cells; K562 cells exhibited no MHC class I expression neither before nor after heat shock. Inhibition of RNA-(actinomycin D)

or

protein-synthesis (cycloheximide) prior to heat treatment completely inhibits the expression of HSP72 on the cell surface of both tumor cells, thus indicating that de novo protein synthesis is required for HSP72 cell surface expression. Since, apart from HSP72, protein synthesis in general is down-modulated by heat shock we speculate that HSP72 mols. that are expressed on the cell surface of tumor cells might be recruited from newly synthesized proteins. The heat-inducible HSP72 cell surface expression on tumor cells could be correlated with an increased sensitivity of leukemic and sarcoma cells to lysis mediated by NK effector cells. The results of cold target inhibition assays revealed that histol. different tumor cells (sarcoma and leukemic cells) that we exposed to non-lethal temps. have to share a similar if not identical HSP72 immunogenic determinant.